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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/674,087	09/29/2003	Jianzhu Chen	0492611-0507 (MIT 10396)	2178

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EXAMINER	
ASHEN, JON BENJAMIN	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/674,087	CHEN ET AL.	
	Examiner	Art Unit	
	Jon B. Ashen	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-97 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-97 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-20, 23-37, 50-62, 72-80 and 91-95, drawn to a composition comprising an RNAi-inducing entity and a delivery agent, classifiable in class 536, subclass 24.5.

II. Claim 22, drawn to a composition comprising a plurality of different siRNAs, shRNAs or RNAi inducing vectors whose presence within a cell results in production of a plurality of different siRNAs or shRNAs targeted to a single target transcript, classifiable in class 536, subclass 24.5.

III. Claim 23, drawn to a composition comprising a plurality of different siRNAs, shRNAs or RNAi inducing vectors whose presence within a cell results in production of a plurality of different siRNAs or shRNAs targeted to different target transcripts, classifiable in class 536, subclass 24.5.

IV. Claims 38-49, 63-71, 81-90 and 96-97, drawn to a method of inhibiting a target transcript in a mammalian subject or of preventing or treating a disease comprising administering a composition comprising an RNAi-inducing entity and a delivery agent, classifiable in class 514, subclass 44.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I-III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). Invention I is drawn to a composition comprising an RNAi-inducing entity and a delivery agent. Invention II is drawn to a composition comprising a plurality of different siRNAs, shRNAs or RNAi inducing vectors (all of which are set forth in the specification as filed as being encompassed by "RNAi inducing entity") whose presence within a cell results in production of a plurality of different siRNAs or shRNAs targeted to a single target transcript. Invention III is drawn to a composition comprising a plurality of different siRNAs, shRNAs or RNAi inducing vectors (all of which are set forth in the specification as filed as being encompassed by "RNAi inducing entity") whose presence within a cell results in production of a plurality of different siRNAs or shRNAs targeted to a different target transcript In the instant case the different inventions are not disclosed as capable of use together and have different modes of operation. The composition of Invention I will operate based on the targeting of a single target transcript by a single RNAi inducing entity (that can be an siRNA, shRNA or vector expression one of the aforementioned). The composition of Invention II will operate based on the targeting of a single target transcript by multiple different siRNAs, shRNAs or RNAi inducing vectors. The composition of Invention III will operate based on the targeting of different target transcripts by multiple, different siRNAs, shRNAs or RNAi inducing vectors.

Furthermore, searching any of inventions I-III together would impose a serious and undue search burden. In the instant case, prior art searches of each composition are not coextensive, as each search must cover the different limitations of what is claimed in each invention. Search of each of these inventions including all recited limitations, would require different key word searches in divergent patent and non-patent literature databases. Each search would then require subsequent in-depth analysis of all relevant prior art literature, placing an undue and serious burden on the Office in terms of both search and examination. As such, it would be burdensome to perform search and examination of any of Inventions I-III together.

3. Inventions I-III and IV are related as products and processes of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). Inventions I-III are relied upon as above. Invention IV is drawn to methods of inhibiting a target transcript in a mammalian subject or of preventing or treating a disease comprising administering a composition comprising an RNAi-inducing entity and a delivery agent. In the instant case, each of the claimed products of inventions I-III can be used in a materially different process of using that product, which would be, for example, an *in vitro* assay of gene function of single or multiple genes or an *in vitro* assay measuring the phenotypic effect of gene silencing on a single or multiple target transcripts.

Furthermore, searching any of Inventions I-III with Invention IV would impose a serious and undue burden. In the instant case, prior art searches of each composition and of methods of treatment comprising administering the claimed compositions, are not coextensive. Search of each of these inventions would require different key word searches of each composition and would include, at least, a search for the distinctive steps required by the method that would not be required by the composition. These searches would need to be performed in divergent patent and non-patent literature databases. The different searches would then require subsequent in-depth analysis of the unrelated prior art literature, placing a serious and undue burden on the Office in terms of both search and examination. As such, it would be burdensome to perform a search and examination of any of Inventions I-III with Invention IV.

4. Groups I and IV are further restricted as follows:

5. Claims 1, 81, 84 and 91 are subject to an additional restriction since each claim is not considered to be presented as a proper genus/Markush. See MPEP 803.02 - PRACTICE RE MARKUSH-TYPE CLAIMS - If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Since the decisions in In re Weber, 580 F.2d 455, 198 USPQ 328 (CCPA 1978) and In re Haas, 580 F.2d

461, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention. In re Harnish, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and Ex parte Hozumi, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claims 1, 81, 84 and 91 specifically claim delivery agents as listed that are a) cationic and modified cationic polymers, b) peptide molecular transporters, c) surfactants suitable for introduction into the lung, d) liposomes, e) non-cationic and modified non-cationic polymers, f) bupivacaine and g) chloroquine (claim 81 additionally lists h) lipopolyplexes). Each of these compounds is patentably distinct because the mode of operation of each of these biologically, functionally, structurally and/or chemically distinct delivery agents is based on the particular chemical structure and properties of that delivery agent and is not shared by the other delivery agents. Additionally, a search of each claimed delivery agent would not be coextensive with a search of any of the other claimed delivery agents because the searches would require different key word and structure searches in divergent patent and non-patent literature databases, placing an undue burden on the examiner to search and examine any of the claimed delivery agents together.

If Applicant chooses to elect the composition of group I or the method of group IV, the claims of the elected group will be examined insofar as they read on the elected subject matter (i.e., the elected delivery agent) that is identified above in a-h.

6. This application contains claims directed to the following patentably distinct species of the claimed invention: Compositions comprising RNAi inducing entities that are a) siRNAs, b) shRNAs, c) lentivirus and lentiviral vectors and d) DNA vectors as set forth in claims 7-10, 13-15, 31-37, 56-62 and 74-80 and methods of treatment that require compositions comprising RNAi inducing entities that are siRNAs, shRNAs, lentivirus and lentiviral vectors and DNA vectors as set forth in claims 42-47 and 64-70. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claims 1, 10, 13, are generic to the claimed compositions. Claims 1, 23, 38, 50, 63 and 72 are generic to all claimed RNAi inducing entities (either comprised in compositions or wherein the composition is required to practice the claimed method). Claims 10, 33, 44, 58, 66 and 76 are generic to the claimed RNAi inducing vectors and encompasses all viral and non viral vectors including DNA vectors. Claims 13, 35, 46, 60, 67, 77 are generic to all viral vectors and DNA vectors (which, in being claimed broadly, can be viral or non-viral) and sub-generic to the claimed RNAi-inducing vectors.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

7. This application contains claims directed to the following patentably distinct species of the claimed invention: The instant compositions comprising an RNAi inducing entity and a delivery agent wherein the delivery agent is a cationic polymer selected from the group of cationic polymers as listed in claim 24.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, claim 23 is generic to the cationic polymers recited in claims 24, 25 and 26.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims

readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

8. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art and would require divergent searches of sequence and literature databases placing an undue administrative burden on the examiner, restriction for examination purposes as indicated is proper.

9. Claim 1 link(s) inventions listed in group I, claim 1 that are the following patentably distinct genera of delivery agents: a) cationic and modified cationic polymers,

b) peptide molecular transporters, c) surfactants suitable for introduction into the lung, d) liposomes, e) non-cationic and modified non-cationic polymers, f) bupivacaine and g) chloroquine. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 1. Claim 1 also link(s) inventions listed in group 1, claims 23, 50 and 72 that are the following patentably distinct genera of delivery agents: a) cationic and modified cationic polymers, c) surfactants suitable for introduction into the lung and b) peptide molecular transporters, respectively. Claim 91 link(s) inventions listed in group IV, claim 91, that are the following patentably distinct genera of compositions comprising RNAi inducing entities and delivery agents wherein the delivery agents are: a) cationic and modified cationic polymers, b) peptide molecular transporters, c) surfactants suitable for introduction into the lung, d) liposomes, e) non-cationic and modified non-cationic polymers, f) bupivacaine or g) chloroquine. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 91. Claim 81 link(s) inventions listed in group IV, claim 81, that are the following patentably distinct genera of methods of treatment requiring administration of compositions comprising RNAi inducing entities and delivery agents wherein the delivery agents are: a) cationic and modified cationic polymers, b) peptide molecular transporters, c) surfactants suitable for introduction into the lung, d) liposomes, e) non-cationic and modified non-cationic polymers, f) bupivacaine, g) chloroquine or h) lipopolyplexes. Claim 81 also link(s) inventions listed in group IV, claims 38 and 63 that are the following patentably distinct genera of methods of treatment requiring administration of compositions comprising RNAi inducing entities

and delivery agents wherein the delivery agents are a) cationic and modified cationic polymers and c) surfactants suitable for introduction into the lung. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 81. Claim 84 and link(s) inventions listed in group IV, claim 84, that are the following patentably distinct genera of methods of treatment requiring administration of compositions comprising RNAi inducing entities and delivery agents wherein the delivery agents are: a) cationic and modified cationic polymers, b) peptide molecular transporters, c) surfactants suitable for introduction into the lung, d) liposomes, e) non-cationic and modified non-cationic polymers, f) bupivacaine or g) chloroquine. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 84. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

10. In summary, Applicant is requested to elect a single patentably distinct composition or method as identified above in Inventions I-IV, wherein the invention is a composition that comprises (inventions I-III) or a method that requires the use of a composition comprising i) a single species of an RNAi-inducing entity (siRNA, shRNA, lentiviral vector or DNA vector) as set forth above and ii) a single patentably distinct genera of delivery agent, identified as a-h above. The elected invention will be examined, in its full scope, including all claims readable thereon.

11. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is

found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon B. Ashen whose telephone number is 571-272-2913. The examiner can normally be reached on 7:30 am - 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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